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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,806	AYDIN, ATAKAN	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *11-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a method for detecting at least one target nucleic acid, classified in class 435, subclass 91.2, for example.

II. Claims 11-21, drawn to a kit, classified in class 536, subclass 23.1, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the methods presented in Claim 1 do not require the use of the products presented in Group II. The methods of Group I can be performed with multiple materially different probes.

Furthermore, searching the inventions of Groups II and I together would impose serious search burden. The inventions of Groups II and I have obtained a separate status in the art as shown by their different classifications. Moreover, since the methods presented in Claim 1 of Group I do not require the products of

Group II, the search of these groups together is not coextensive. A search for the methods of Group I would not necessarily result in any of the products of Group II. As such, it would be burdensome to search the inventions of Groups I and II together.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction

requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Andrew Finn on January 11, 2006 a provisional election was made without traverse to prosecute the invention of Group I, Claims 1-10. Affirmation of this election must be made by applicant in replying to this Office action. Claims 11-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship

must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The abstract of the disclosure is objected to because it does not appropriately describe the invention. Correction is required. See MPEP § 608.01(b).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that only representative claims will be discussed.

1. Claims 1-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-28 of copending application Andersen et al. (10/665671).

Claim 1 of Andersen et al. recite a method for detecting at least one target nucleic acid sequence in a sample comprising: forming a ligation reaction composition comprising the sample and a ligation probe set for each target nucleic acid sequence, the probe set comprising (a) at least one first probe,

comprising a target-specific portion, a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence, and a first addressable portion located between the 5' primer-specific portion and the target-specific portion, wherein the first addressable portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion, a 3' primer-specific portion, wherein the 3' primer-specific portion comprises a sequence, and a second addressable portion located between the 3' primer-specific portion and the target-specific portion, wherein the second addressable portion comprises a sequence, wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target nucleic acid sequence; forming a test composition by subjecting the ligation reaction composition to at least one cycle of ligation, wherein adjacently hybridizing complementary probes are ligated to one another to form a ligation product comprising the 5' primer-specific portion, the first addressable portion, the target-specific portions, the second addressable portion, and the 3' primer-specific portion; forming an amplification reaction composition comprising: the test composition; a polymerase; a first labeled probe, wherein the first labeled probe has a first detectable signal value when it is not hybridized to a complementary sequence, and wherein the first labeled probe comprises the sequence of the first addressable portion or comprises a sequence complementary to the sequence of the first addressable portion; a second labeled probe, wherein the second labeled probe has a first detectable signal value when it is not hybridized to a complementary sequence, and wherein the second labeled probe comprises the

sequence of the second addressable portion or comprises a sequence complementary to the sequence of the second addressable portion; and at least one primer set, the primer set comprising (i) at least one first primer comprising the sequence of the 5' primer-specific portion of the ligation product, and (ii) at least one second primer comprising a sequence complementary to the sequence of the 3' primer-specific portion of the ligation product; subjecting the amplification reaction composition to at least one amplification reaction; and detecting a second detectable signal value from the first labeled probe and from the second labeled probe at least one of during and after the amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value of the first labeled probe and a threshold difference between the first detectable signal value and the second detectable signal value of the second labeled probe indicates the presence of the target nucleic acid sequence; and wherein no threshold difference between the first detectable signal value and the second detectable signal value of the first labeled probe and no threshold difference between the first detectable signal value and the second detectable signal value of the second labeled probe indicates the absence of the target nucleic acid sequence.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive concept of detecting a target nucleic acid comprising a ligation detection reaction further comprising detecting threshold difference of detectable signals.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claims 1-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-48 of copending application Friedlander et al. (10/693609).

Friedlander et al. recite a method for detecting the presence or absence of at least one target nucleic acid sequence in a sample comprising: forming a ligation reaction composition comprising the sample, and a ligation probe set for each target nucleic acid sequence, the probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion and a 3' primer-specific portion, wherein the 3' primer-specific portion comprises a sequence, wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target sequence; forming a test composition by subjecting the ligation reaction composition to at least one cycle of ligation, wherein adjacently hybridizing complementary probes are ligated to one another to form a ligation product comprising the 5' primer-specific portion, the target-specific portions, and the 3' primer-specific portion; forming at least one amplification reaction composition comprising: at least a portion of the test composition; a polymerase; a double-stranded-dependent specific label, wherein

the double-stranded-dependent label has a first detectable signal value when the double-stranded-dependent label is not exposed to double-stranded nucleic acid; and at least one primer set, the primer set comprising (i) at least one first primer comprising the sequence of the 5' primer-specific portion of the ligation product, and (ii) at least one second primer comprising a sequence complementary to the sequence of the 3' primer-specific portion of the ligation product; subjecting the at least one amplification reaction composition to at least one amplification reaction; and detecting a second detectable signal value at least one of during and after the at least one amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value indicates the presence of the target nucleic acid sequence, and wherein no threshold difference between the first detectable signal value and the second detectable signal value indicates the absence of the target nucleic acid sequence.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive concept of detecting a target nucleic acid comprising a ligation detection reaction further comprising detecting threshold difference of detectable signals.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (U.S. 6,027,889) in view of Godfrey et al. "Quantitative mRNA Expression Analysis from Formalin-Fixed, Paraffin-Embedded Tissues Using 5' Nuclease Transcription-Polymerase Chain Reaction" Journal of Molecular Diagnostics. 2000. Vol. 2, No. 2: Pages 84-91).

With regard to Claims 1 and 10, Barany et al. discloses a method for detecting the at least one target nucleic acid sequence in a sample (Figures 8-12; Columns 9-11; Columns 23-30; Column 41, Example 4, for example) comprising a method for detecting at least one target nucleic acid sequence in a sample comprising: forming a ligation reaction composition comprising the sample and a ligation probe set for each target nucleic acid sequence, the probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion and a 3' primer-specific portion, wherein the 3' primer-specific portion

comprises a sequence, wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target nucleic acid sequence, and wherein one probe in each probe set further comprises an addressable portion located between the primer-specific portion and the target-specific portion, wherein the addressable portion comprises a sequence.

Barany et al. disclose a subsequent amplification step with labeled primers (Figure 11,12; Columns 24,25, for example), however, does not expressly disclose employing real-time detection methods or detection through comparing threshold values.

Godfrey et al. disclose methods for comparing real-time detection values (Abstract; Page 86, Column 2; Page 87, Column 1). They expressly disclose detecting differences in threshold values to quantify the amount of PCR target (Page 86, Column 1, for example).

Based on the combined disclosures of the applied references, it would have obvious to one of ordinary skill in the art at the time of invention to modify the ligation dependent reaction/amplification (i.e. LDR/PCR) methods of Barany et al. to incorporate real-time detection methods. It would have been further obvious to one of ordinary skill in the art at the time of invention to detect the presence of a particular nucleic acid sample by comparing threshold values based on signals from double-stranded dependent labels. A practitioner of ordinary skill in the art would have recognized that if a particular probe set failed to ligate due to a particular nucleotide mismatch (i.e. SNP or allele), it would fail

to produce a threshold value in subsequent amplification reactions (and vice versa) thereby allowing one to determine a particular allele at a given locus (i.e. heterozygosity or homozygosity) by comparison of threshold values. At the time of invention, the disclosure of Barany et al. and Godfrey et al. clearly would have provided the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

With regard to Claims 2-5, Godfrey et al. discloses real-time quantitative amplification methods utilizing fluorescent 5' nuclease probes (Page 86, Column 1, for example).

With regard to Claims 6-9, Godfrey et al. discloses real-time quantitative amplification methods utilizing fluorescent hybridization dependent probes (Page 86, Column 1, for example).

Conclusion

Claims 1-10 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

1/16/06

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1/19/06